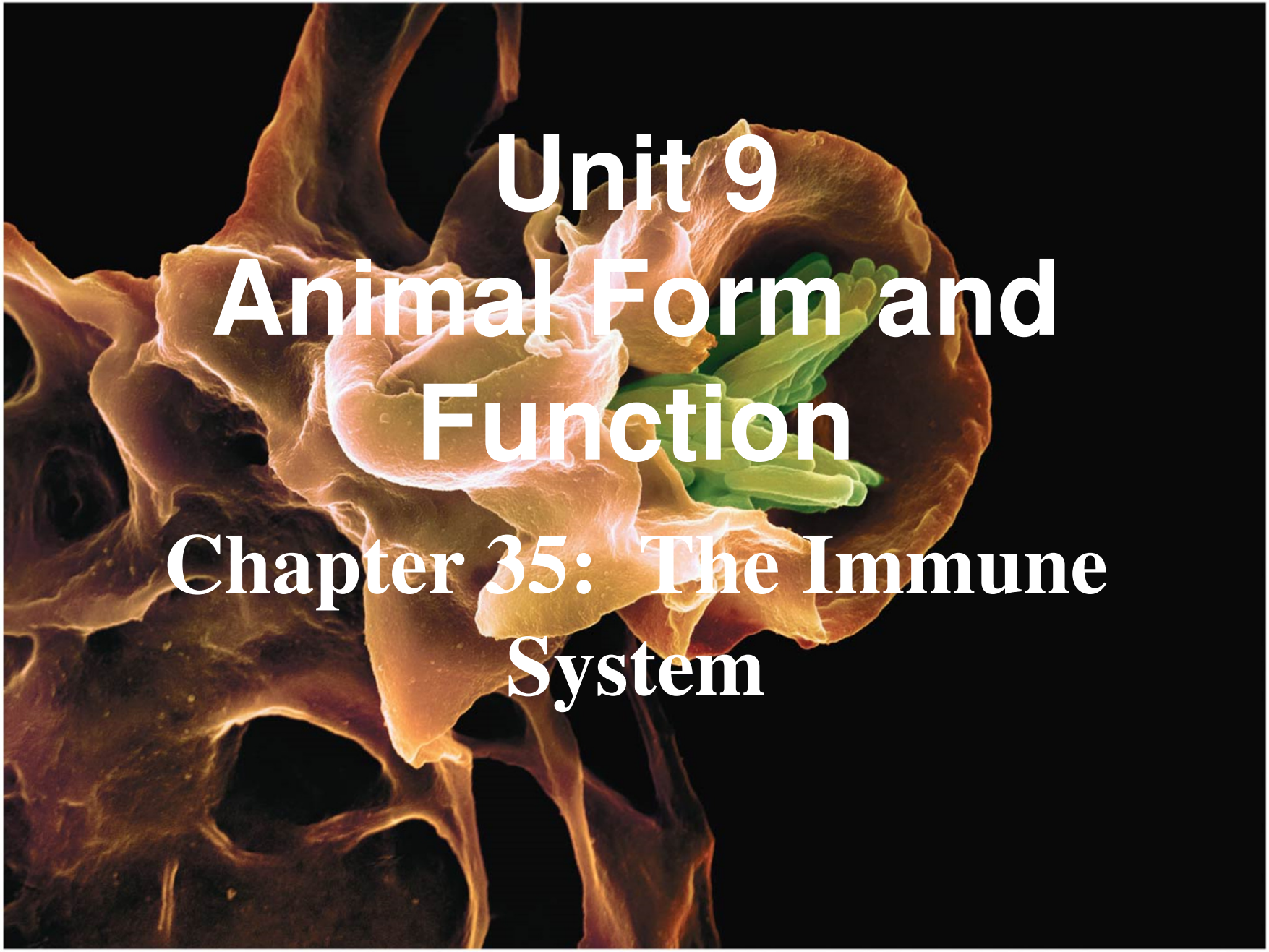


Unit 9
Animal Form and Function

Chapter 35: The Immune System

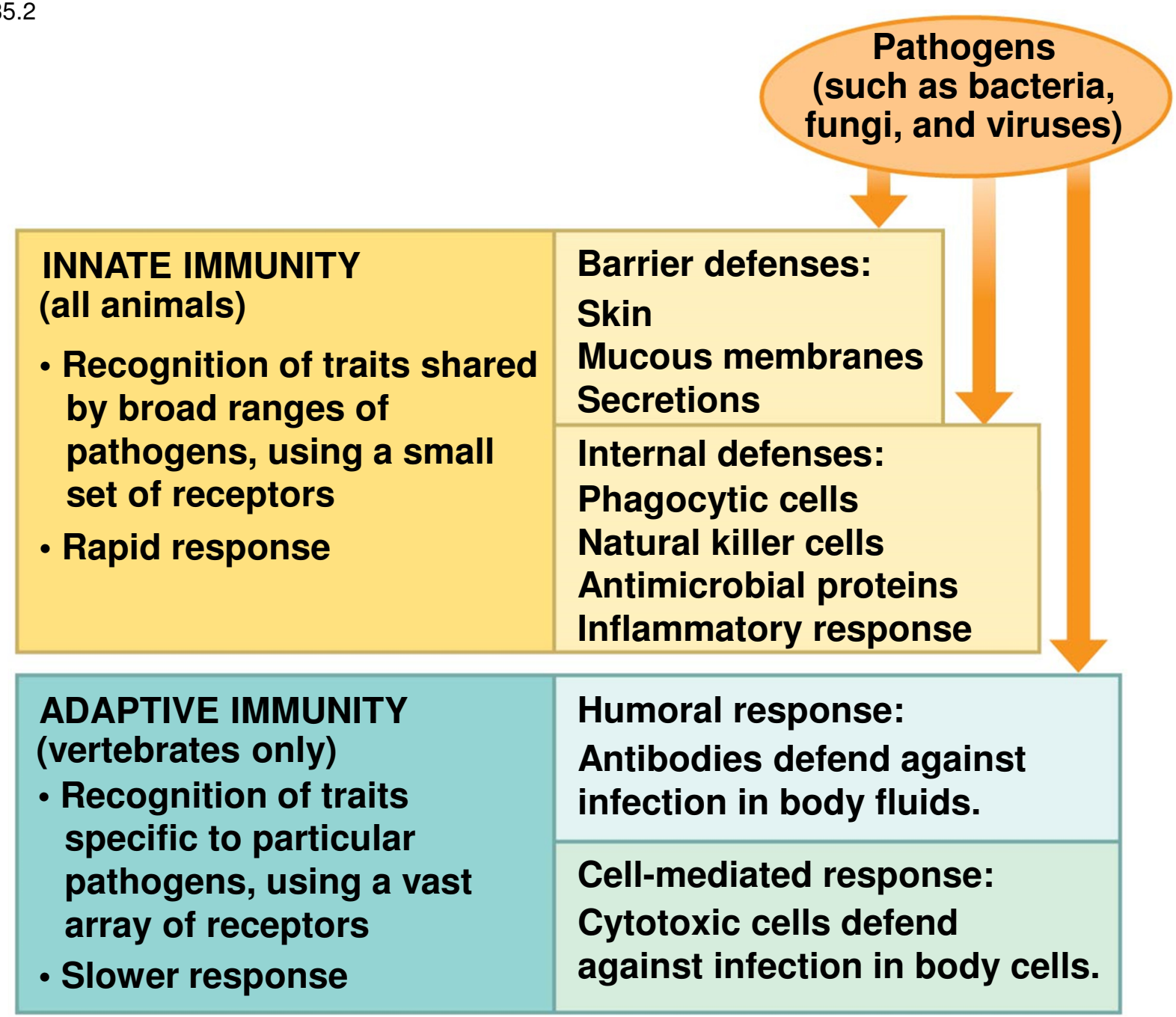
Overview: Recognition and Response

- **Pathogens** are agents that cause disease
  - Ex: Bacteria, fungus, virus, etc
  - Infect a wide range of animals, including humans
- The **immune system** enables an animal to avoid or limit many infections
  - First line of defense is to help prevent pathogens from gaining entrance to body
  - If the pathogen enters, immune system must distinguish the foreign particles/cells from its own

- All animals have **innate immunity**
  - Defense that is active immediately upon infection
  - Present before any exposure to pathogens and is effective from the time of birth
  - Involves nonspecific responses to pathogens
    - Recognition of traits shared by broad range of pathogens
    - Small set of receptors
  - Rapid response
  - Consists of external barriers plus internal cellular and chemical defenses

- Vertebrates also have **adaptive immunity**
  - Also known as acquired immunity
  - Develops after exposure to agents such as microbes, toxins, or other foreign substances
  - Involves a very specific response to pathogens
    - Vast array of receptors
  - Slower response
  - Consists of humoral and cell-mediated responses

Figure 35.2


Pathogens (such as bacteria, fungi, and viruses)
INNATE IMMUNITY (all animals)
• Recognition of traits shared by broad ranges of pathogens, using a small set of receptors
• Rapid response
Barrier defenses:
Skin
Mucous membranes
Secretions
Internal defenses:
Phagocytic cells
Natural killer cells
Antimicrobial proteins
Inflammatory response
ADAPTIVE IMMUNITY (vertebrates only)
• Recognition of traits specific to particular pathogens, using a vast array of receptors
• Slower response
Humoral response:
Antibodies defend against infection in body fluids.
Cell-mediated response:
Cytotoxic cells defend against infection in body cells.

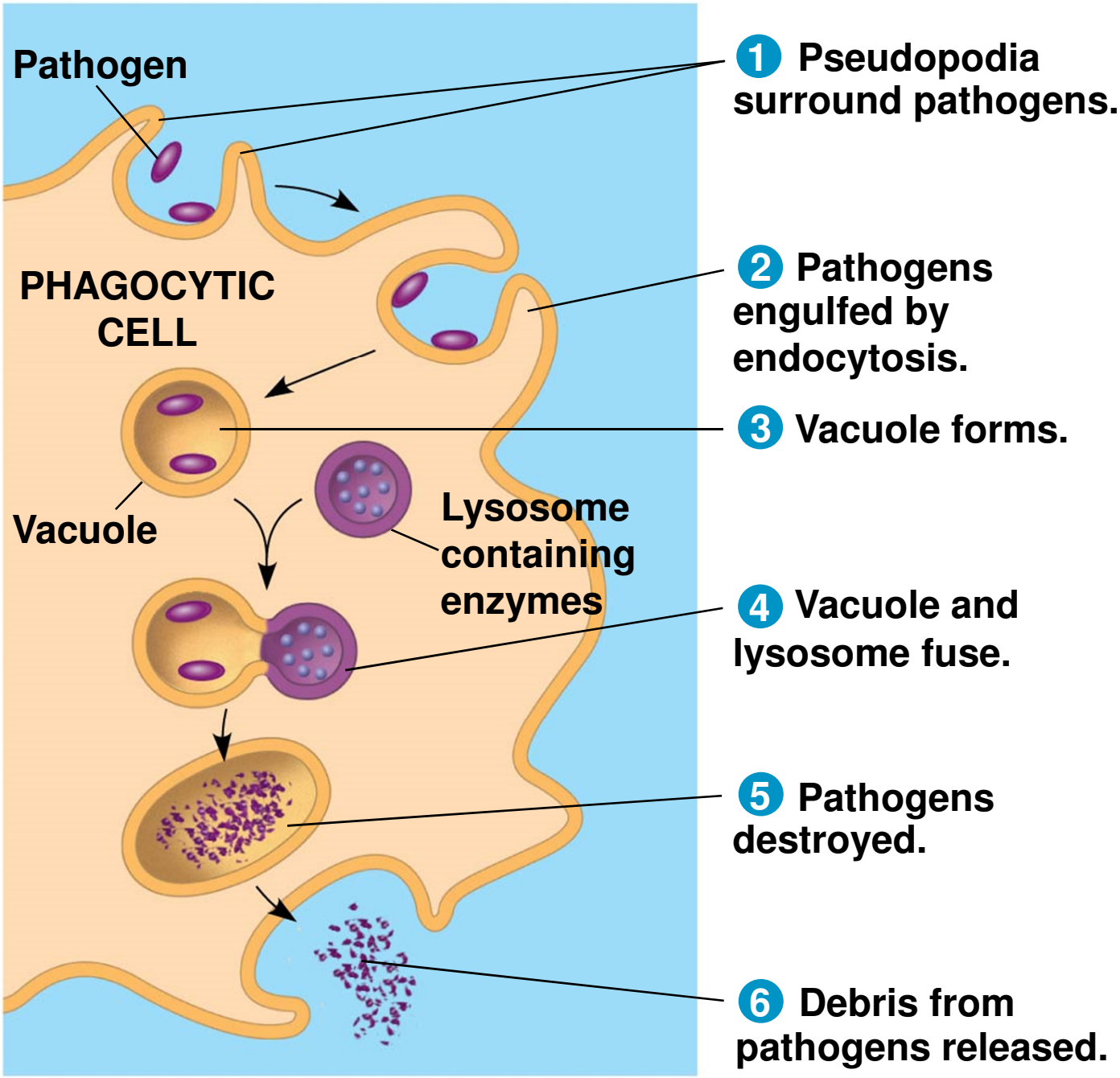
Concept 35.1: In innate immunity, recognition and response rely on traits common to groups of pathogens

- Innate immunity is found in all animals and plants
- In vertebrates, innate immunity is a first response to infections and serves as the foundation of adaptive immunity

Innate Immunity of Invertebrates

- Insects rely on their exoskeleton as a first line of defense against infection
- In the digestive system, the enzyme **lysozyme** breaks down bacterial cell walls, protecting against pathogens ingested along with food
- *Hemocytes* circulate within hemolymph and carry out **phagocytosis**
  - Ingestion and breakdown of foreign substances including bacteria
- The immune system recognizes bacteria and fungi by structures on their cell walls
- An immune response is specific for each class of pathogen

Figure 35.3


Pathogen
PHAGOCYTIC CELL
Vacuole
Lysosome containing enzymes
1 Pseudopodia surround pathogens.
2 Pathogens engulfed by endocytosis.
3 Vacuole forms.
4 Vacuole and lysosome fuse.
5 Pathogens destroyed.
6 Debris from pathogens released.

Innate Immunity of Vertebrates

- Innate defenses include
  - Barrier defenses
  - Phagocytosis
  - Antimicrobial peptides
- Additional defenses are unique to vertebrates
  - Natural killer cells
  - Interferons
  - Inflammatory response

Barrier Defenses

- Barrier defenses include the skin and mucous membranes of the respiratory, urinary, and reproductive tracts
- Mucus traps and allows for the removal of microbes
- Many body fluids including saliva, mucus, and tears are hostile to many microbes
- The low pH of skin and the digestive system prevents growth of many bacteria

Cellular Innate Defenses

- Pathogens entering the mammalian body are subject to phagocytosis
- Phagocytic cells recognize groups of pathogens by **Toll-like receptors** (**TLRs**)
  - Each mammalian TLR binds to fragments of molecules characteristic to a set of pathogens
- Detection of foreign particles triggers phagocytosis and destruction

- There are two main types of phagocytic cells in mammals
  - **Neutrophils**
    - Circulate in the blood and are attracted by signals from infected tissues
  - **Macrophages**
    - Larger phagocytic cells found throughout the body

- Two additional types of phagocytic cells
  - *Dendritic cells*
    - Stimulate development of adaptive immunity in cells that contact the environment (such as skin)
  - *Eosinophils*
    - Discharge destructive enzymes beneath mucosal surfaces
    - Important in defending against mulitcellular invaders

- Cellular innate defenses in vertebrates also involve **natural killer cells**
  - Circulate through the body and detect abnormal cells
  - Do not engulf cells
    - Release chemicals leading to cell death
    - Inhibits the spread of virally infected or cancerous cells
- Many cellular innate defenses involve the lymphatic system

Antimicrobial Peptides and Proteins

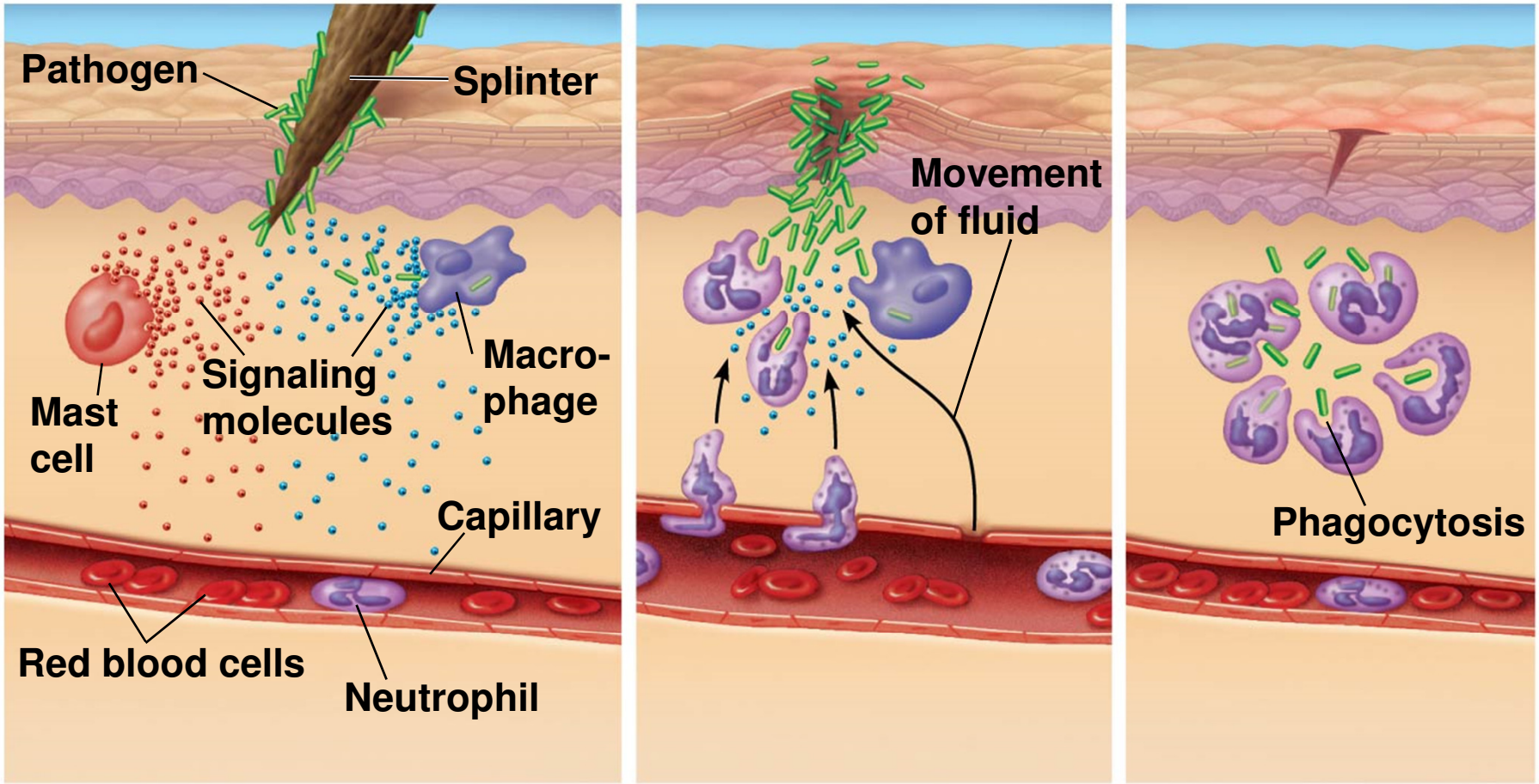
- In mammals, pathogen recognition triggers release of peptides and proteins that attack pathogens or impede their reproduction
- **Interferons** are proteins that provide innate defense by interfering with viruses and helping activate macrophages
  - Limit cell-to-cell spread of viruses
- The **complement system** consists of about 30 proteins that are activated by substances on microbe surfaces
  - Activation can lead to lysis of invading cells

Inflammatory Response

- The **inflammatory response** is brought about by molecules released upon injury of infection
  - Causes pain and swelling
- **Mast cells** release **histamine**
  - Triggers blood vessels to dilate and become more permeable

- Activated macrophages and neutrophils release **cytokines**
  - Signaling molecules that promote blood flow to the site of injury or infection
- Enhanced blood flow to the site helps deliver antimicrobial peptides
  - Results in an accumulation of pus
    - Fluid rich in white blood cells, dead pathogens, and cell debris from damaged tissues

Figure 35.5-3



1 Histamines and cytokines released. Capillaries dilate.

2 Antimicrobial peptides enter tissue. Neutrophils are recruited.

3 Neutrophils digest pathogens and cell debris. Tissue heals.

- Inflammation can be either local or systemic (throughout the body)
  - Fever is a systemic inflammatory response triggered by substances released by macrophages
- *Septic shock* is a life-threatening condition caused by an overwhelming inflammatory response
- Chronic inflammation can also threaten human health
  - Crohn's disease
  - Ulcerative colitis

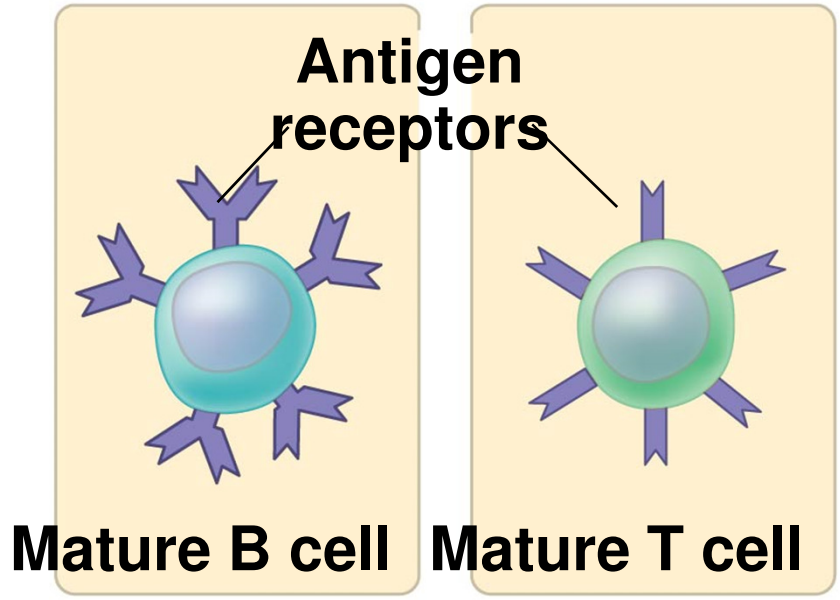
Evasion of Innate Immunity by Pathogens

- Adaptations have evolved in some pathogens that enable them to avoid destruction by phagocytic cells
  - Tuberculosis (TB) resists breakdown within lysosomes after being engulfed by a host cell
- Mechanisms like this make certain fungi and bacteria substantial pathogenic threats

Concept 35.2: In adaptive immunity, receptors provide pathogen-specific recognition

- Vertebrates have adaptive immunity in addition to innate immunity
- The adaptive response relies on two types of **lymphocytes**, or white blood cells

1. Lymphocytes that mature in the **thymus** above the heart are called **T cells**
2. Those that mature in bone marrow are called **B cells**



- **Antigens** are substances that can elicit a response from a B or T cell
  - Ex: Bacterial or viral proteins
- Recognition occurs when a B or T cell binds to an antigen, via an **antigen receptor**
  - Specific!
    - Like lock and key
- The small accessible part of an antigen that binds to an antigen receptor is called an **epitope**

Antigen Recognition by B Cells and Antibodies

- Each B cell antigen receptor is a Y-shaped molecule with two identical **heavy chains** and two identical **light chains**
- Binding of a B cell antigen receptor to an antigen is an early step in B cell activation
  - This gives rise to cells that secrete a soluble form of the protein called an **antibody** or **immunoglobulin**
- Secreted antibodies are similar to B cell receptors but are not membrane bound
- The antibodies, rather than B cells themselves, defend against pathogens!

Figure 35.6

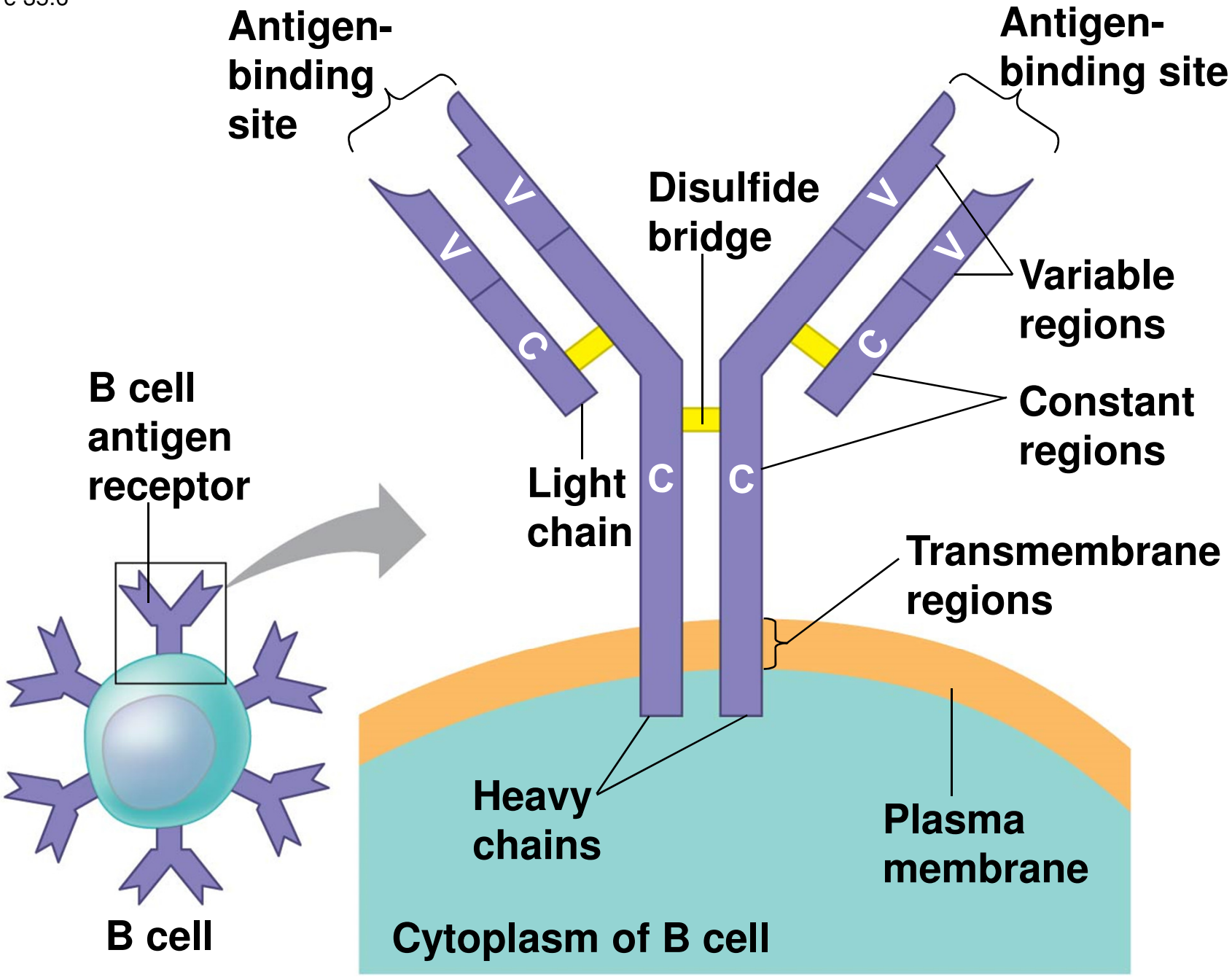
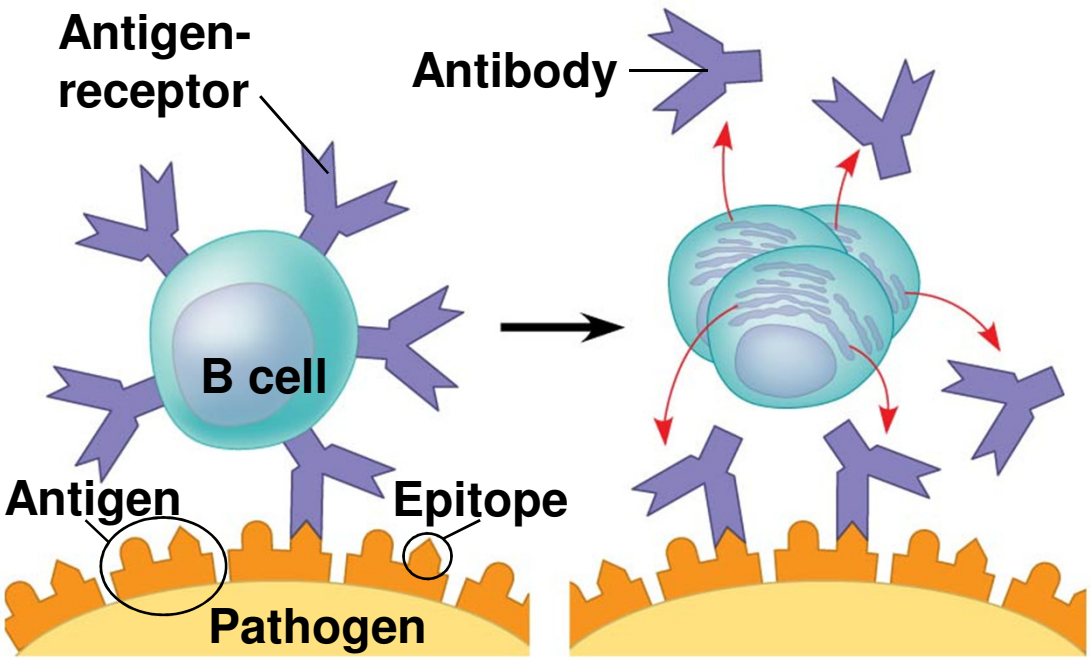
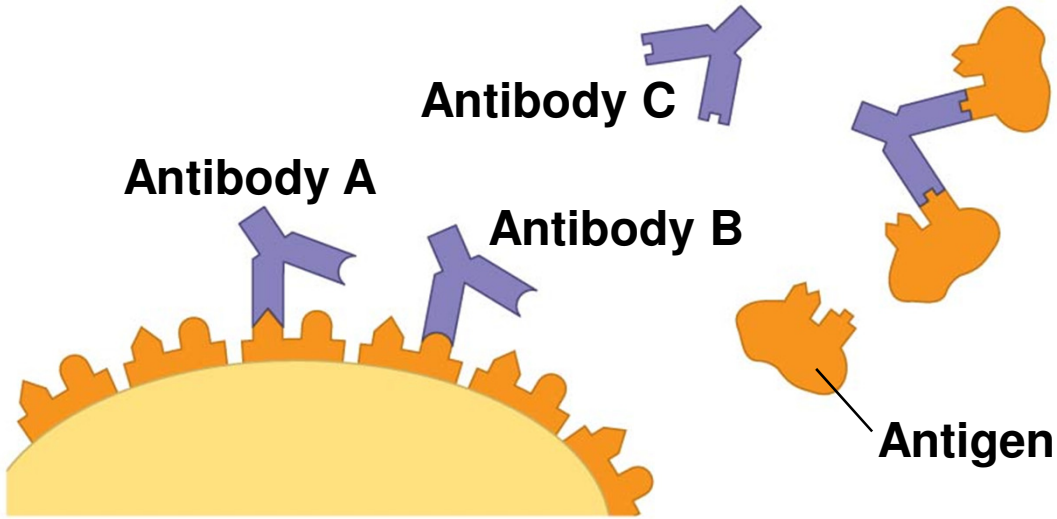

Antigen-binding site
Antigen-binding site
Disulfide bridge
V
V
V
V
C
C
C
C
Variable regions
Constant regions
B cell antigen receptor
Light chain
Transmembrane regions
Heavy chains
Plasma membrane
B cell
Cytoplasm of B cell

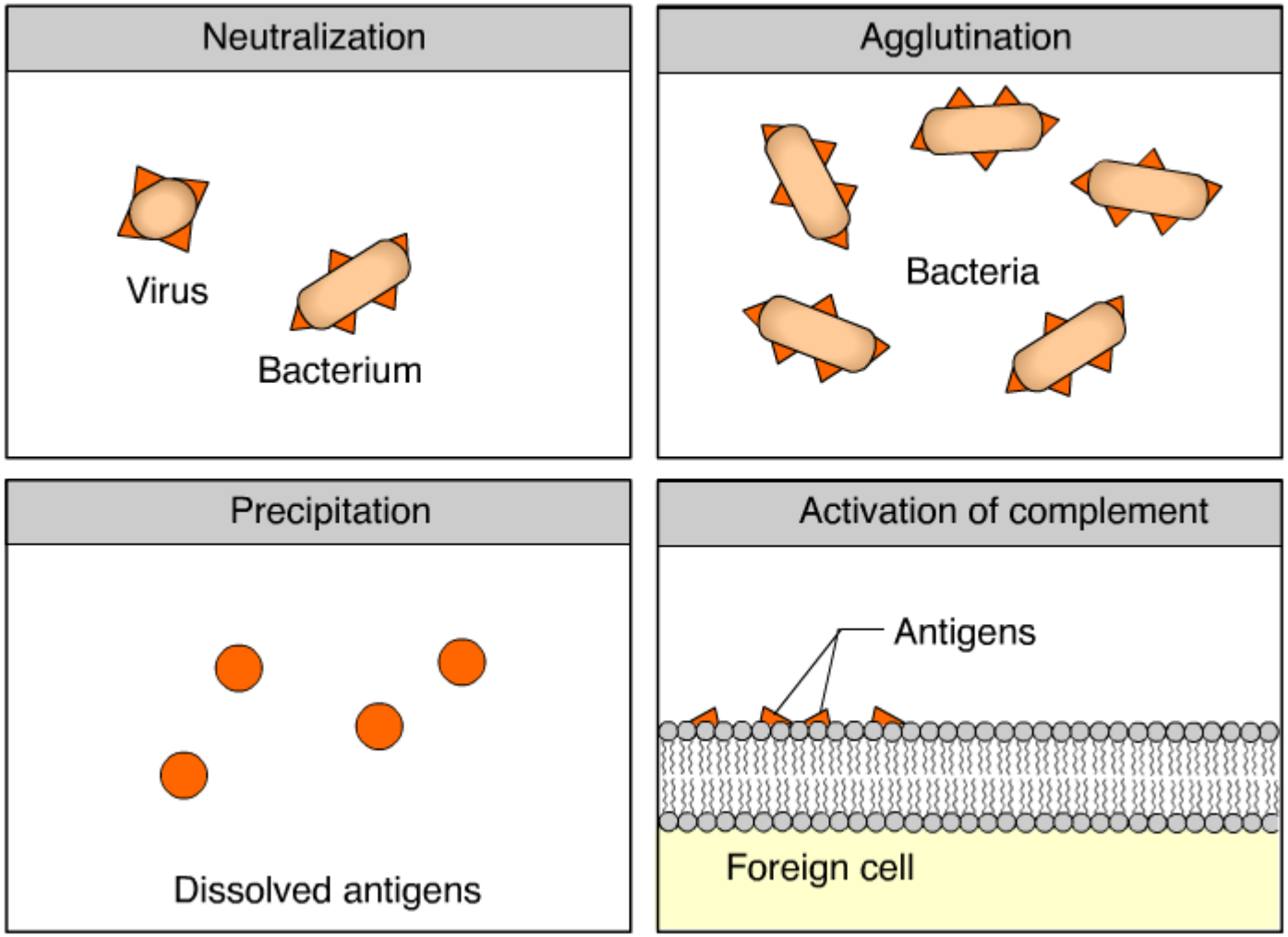
Figure 35.7



(a) B cell antigen receptors and antibodies



(b) Antigen receptor specificity

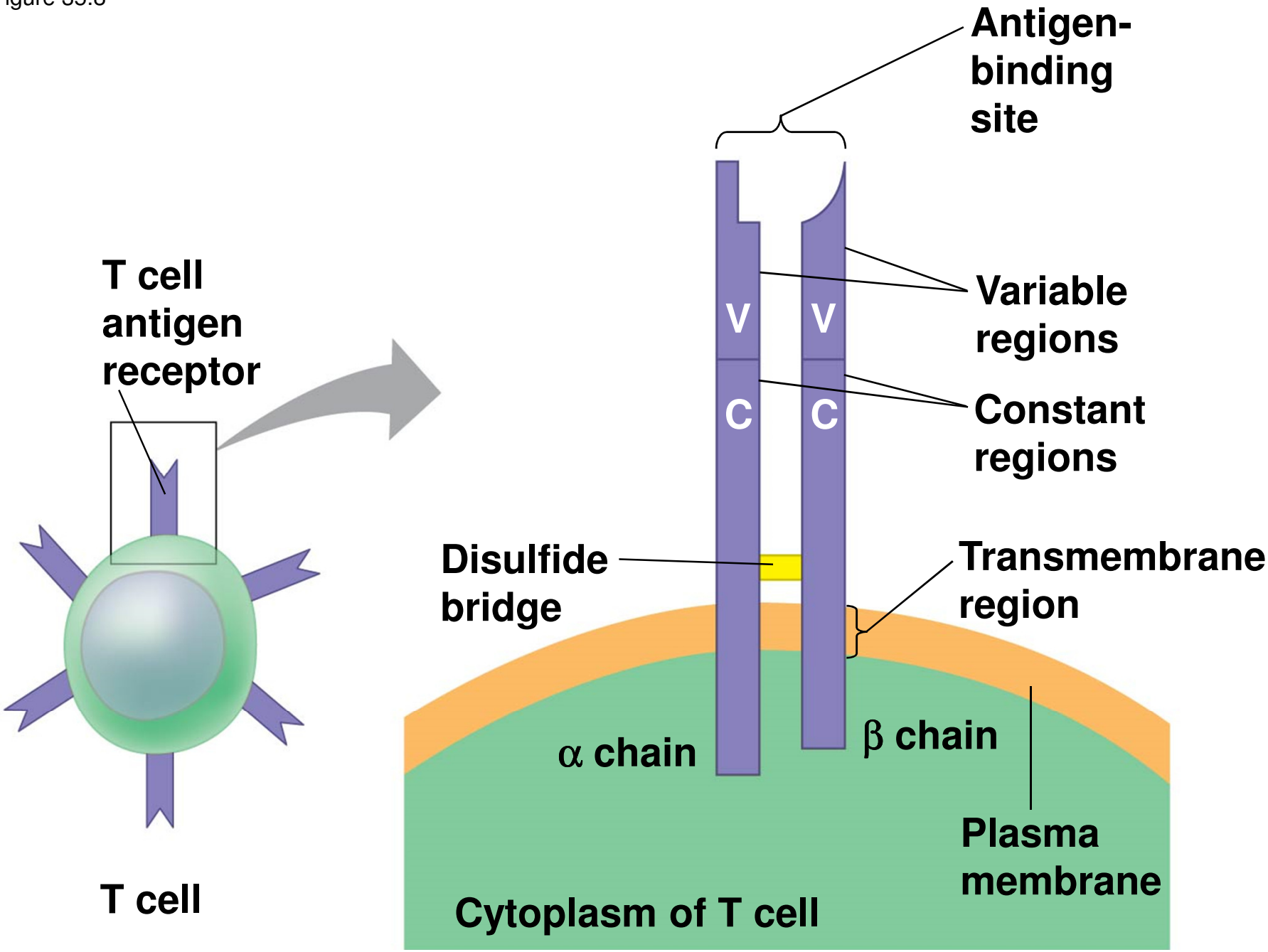


Animation: Antibodies
Right click slide / Select play

Antigen Recognition by T Cells

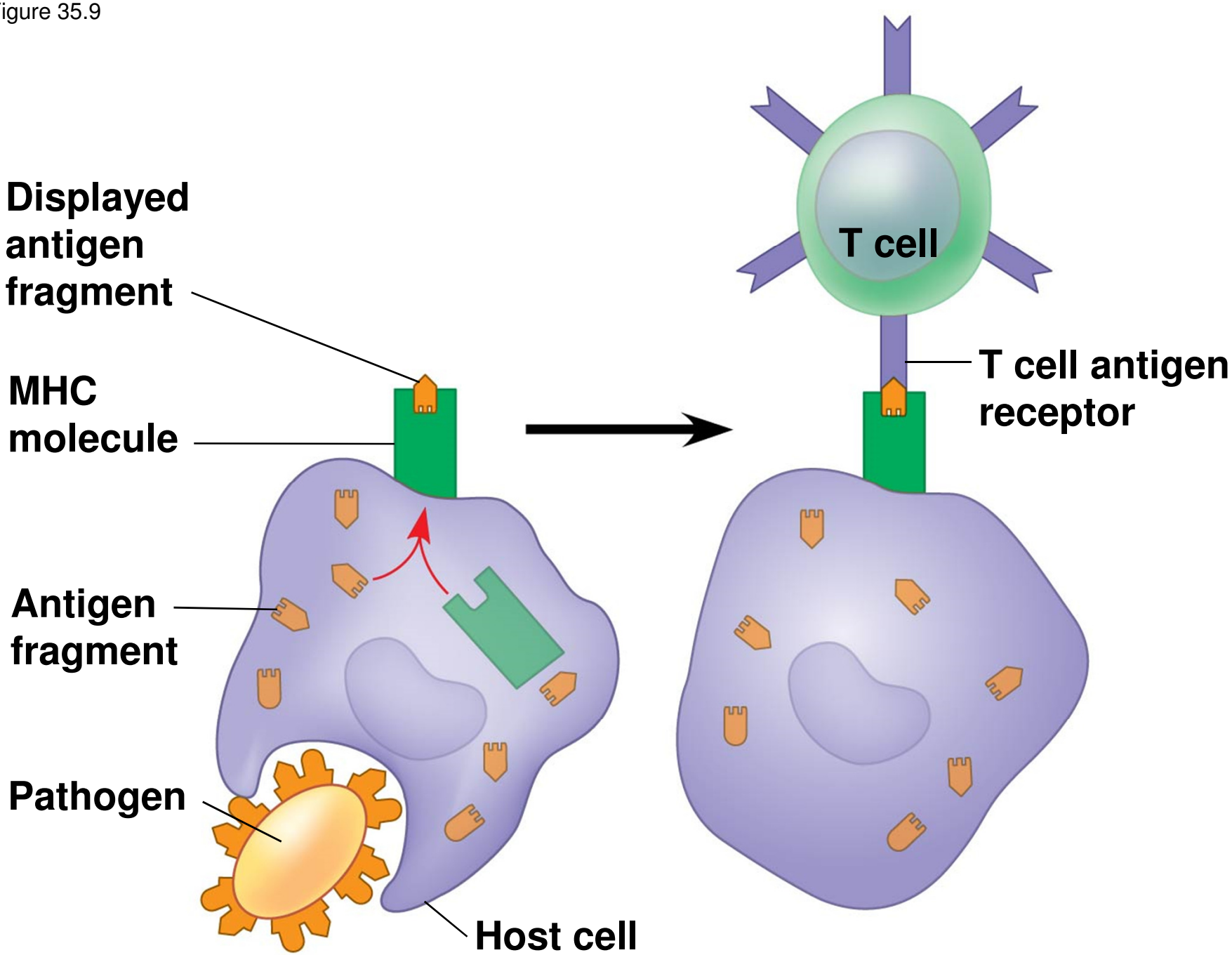
- Each T cell receptor consists of two different polypeptide chains (called α and β)
- T cells bind only to antigen fragments displayed or presented on a host cell
  - Host protein that displays the antigen fragments on the cell surface is called a **MHC (major histocompatibility complex)**

Figure 35.8


Antigen-binding site
T cell antigen receptor
V
V
C
C
Variable regions
Constant regions
Disulfide bridge
Transmembrane region
α chain
β chain
Plasma membrane
T cell
Cytoplasm of T cell

- In infected cells, antigens are cleaved into smaller peptides by enzymes
- MHC molecules bind and transport the antigen fragments to the cell surface
  - Called **antigen presentation**
    - Advertises the fact that a host cell contains a foreign substance!
- A T cell can then bind both the antigen fragment and the MHC molecule
  - This interaction is necessary for the T cell to participate in the adaptive immune response

Figure 35.9


Displayed antigen fragment
MHC molecule
Antigen fragment
Pathogen
Host cell
T cell
T cell antigen receptor

B Cell and T Cell Development

- The adaptive immune system has four major characteristics
  1. Diversity of lymphocytes and receptors
     - Enables immune system to detect pathogens never before encountered
  2. Self-tolerance
     - Lack of reactivity against an animal's own molecules

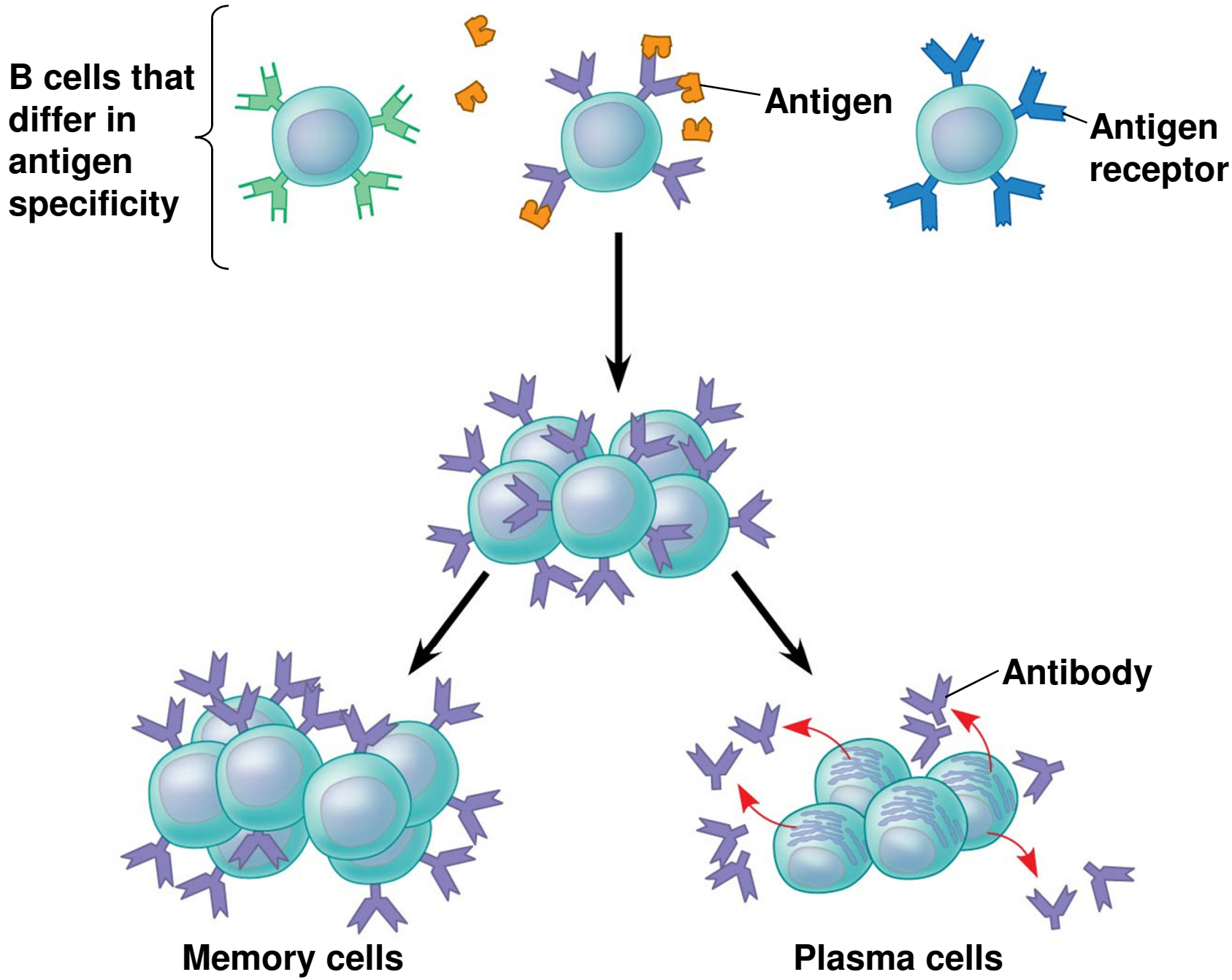
3. Proliferation of B and T cells after activation
   - Increases number of B and T cells specific for an antigen
4. Immunological memory
   - Stronger, more rapid response to antigen encountered previously

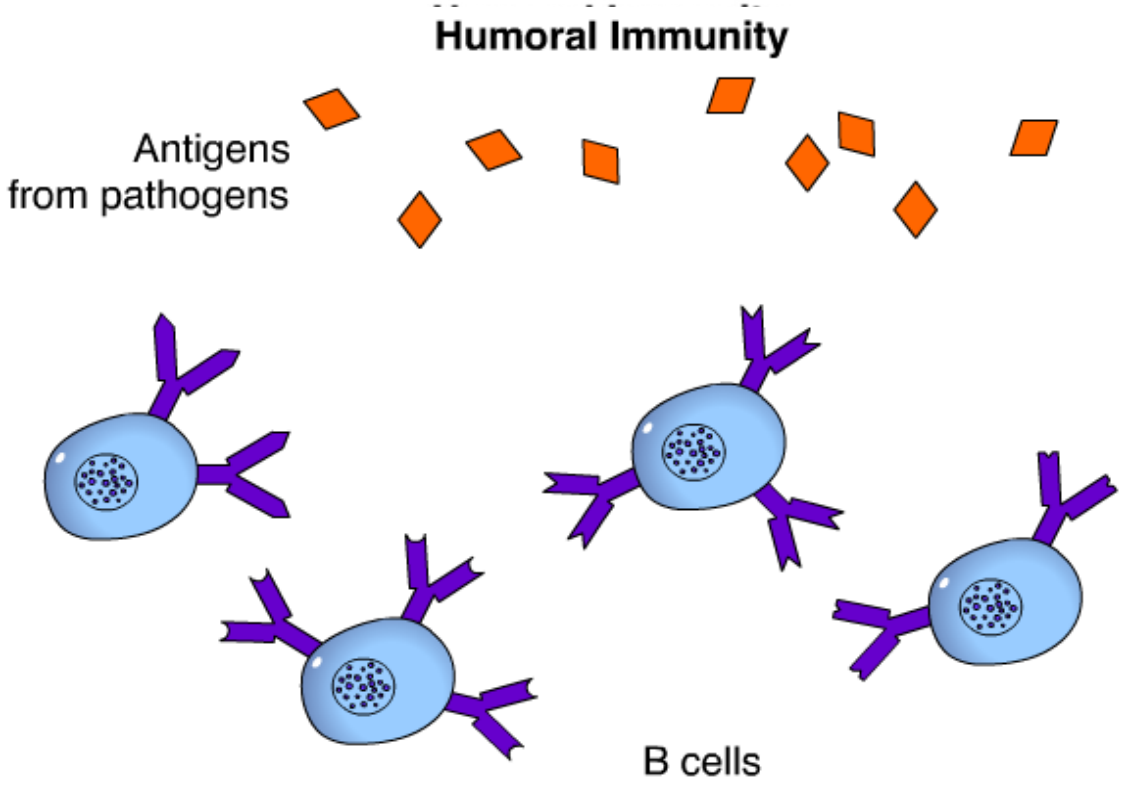
Proliferation of B Cells and T Cells

- In the body only a tiny fraction of antigen receptors are specific for a given epitope
- In the lymph nodes, an antigen is exposed to a steady stream of lymphocytes until a match is made
- This binding of a mature lymphocyte to an antigen initiates events that activate the lymphocyte
- Once activated, a B or T cell undergoes multiple cell divisions to produce a clone of identical cells
  - Called **clonal selection**
    - An encounter with an antigen <u>selects</u> which lymphocyte will divide to produce a <u>clonal</u> population

- Two types of clones are produced
  - **Effector cells**
    - Act immediately against the antigen
    - Short-lived
    - Effector form of B cells are called **plasma cells**
      - Secrete antibodies
    - Effector form of T cells are
      - Helper T cells
      - Cytotoxic T cells
  - **Memory cells**
    - Can give rise to effector cells if the same antigen is encountered again
    - Long-lived

Figure 35.11


B cells that differ in antigen specificity
Antigen
Antigen receptor
Antibody
Memory cells
Plasma cells



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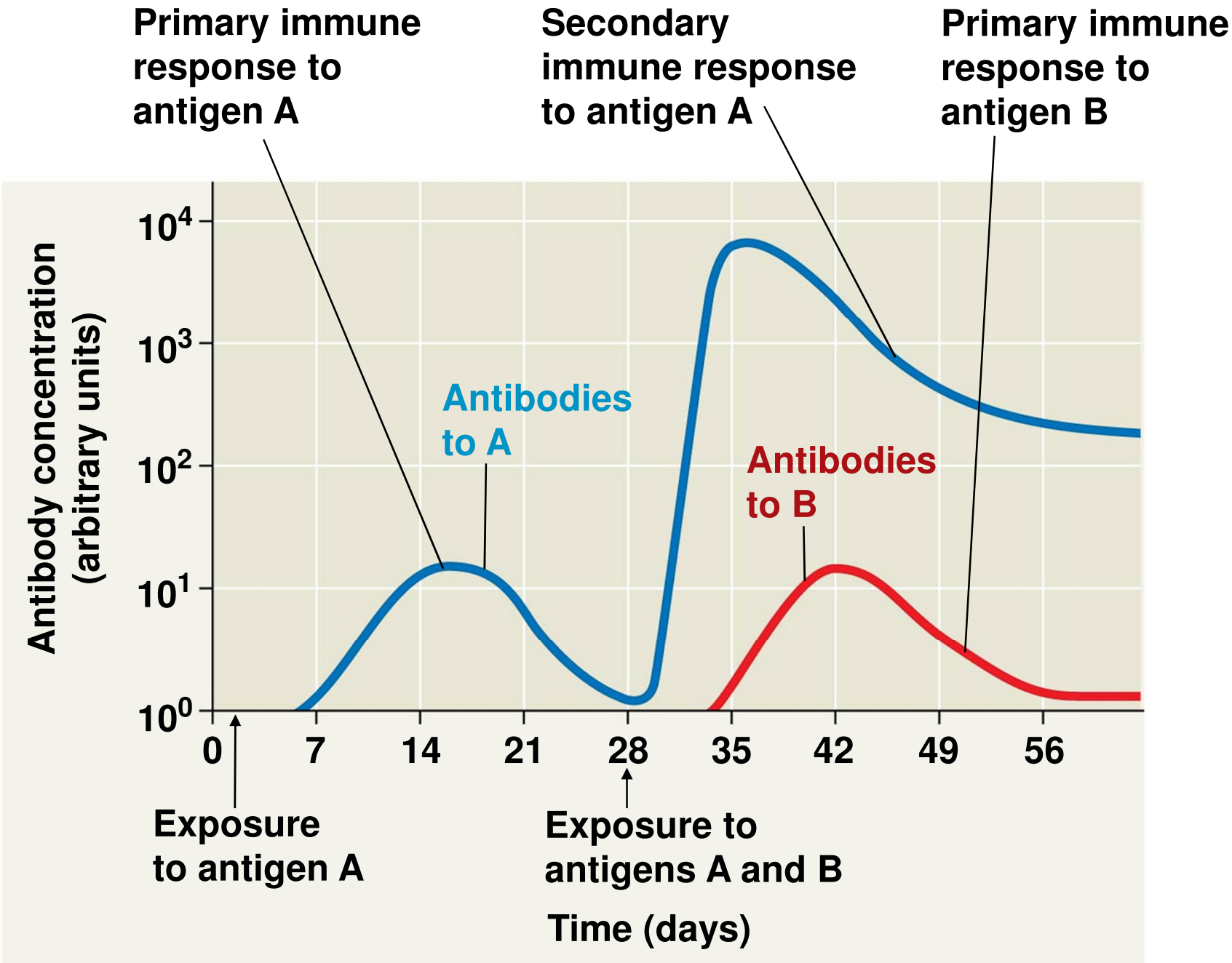
Animation: Role of B Cells
Right click slide / Select play

Immunological Memory

- Immunological memory is responsible for long-term protections against diseases, due to a prior infection
- The first exposure to a specific antigen represents the **primary immune response**
  - Selected B and T cells give rise to their effector forms
- In the **secondary immune response**, memory cells facilitate a faster, stronger, and longer response
  - Occurs if individual is exposed again to same antigen
  - Hallmark of adaptive immunity!

Figure 35.12


Primary immune response to antigen A
Secondary immune response to antigen A
Primary immune response to antigen B
Antibody concentration (arbitrary units)
10^4
10^3
10^2
10^1
10^0
Antibodies to A
Antibodies to B
0
7
14
21
28
35
42
49
56
Exposure to antigen A
Exposure to antigens A and B
Time (days)

Concept 35.3: Adaptive immunity defends against infection of body fluids and body cells

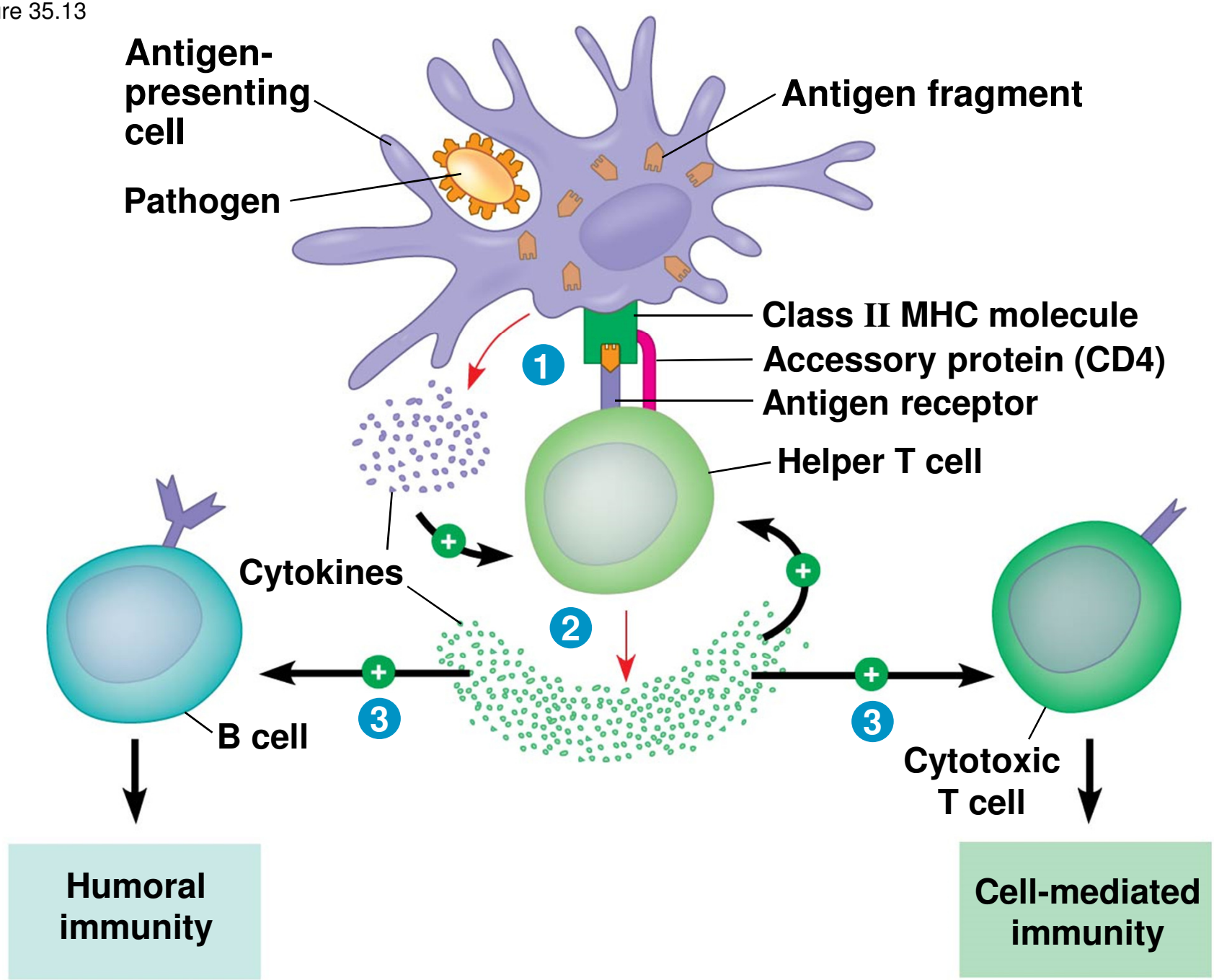
- B and T lymphocytes produce a humoral immune response and a cell-mediated immune response
- In the **humoral immune response,** antibodies help neutralize or eliminate toxins and pathogens in the blood and lymph
- In the **cell-mediated immune response** specialized T cells destroy infected host cells
- Both include a primary and secondary immune response

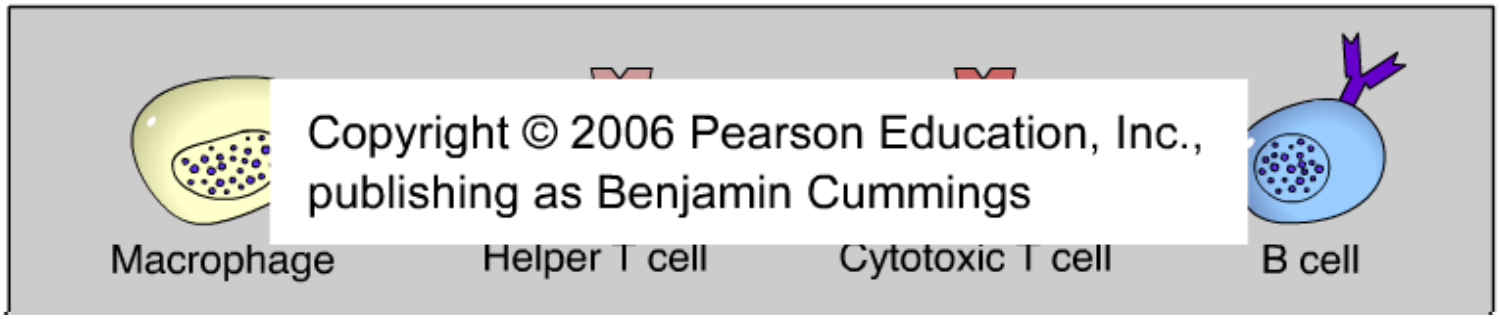
Helper T Cells: A Response to Nearly All Antigens

- A type of T cell called a **helper T cell** triggers both the humoral and cell-mediated immune responses
  - Helper T cells themselves do not carry out the responses
  - Helper T cells produce signals that:
    - Initiate production of antibodies (humoral)
    - Activate T cells (cell-mediated)

- An antigen must be displayed on the surface of an **antigen-presenting cell** and bind specifically to the antigen receptor of a T cell
  - Antigen-presenting cell can be a dendritic cell, macrophage, or B cell
- The helper T cell is activated, proliferates, and forms a clone of helper T cells, which in turn
  - Activate the appropriate B cells
    - Humoral immunity: Secretion of antibodies by plasma cells
  - Help stimulate cytotoxic T cells
    - Cell mediated immunity: Attack infected cells

Figure 35.13


Antigen-presenting cell
Pathogen
Antigen fragment
Class II MHC molecule
Accessory protein (CD4)
Antigen receptor
Helper T cell
1
Cytokines
2
3
3
B cell
Cytotoxic T cell
Humoral immunity
Cell-mediated immunity



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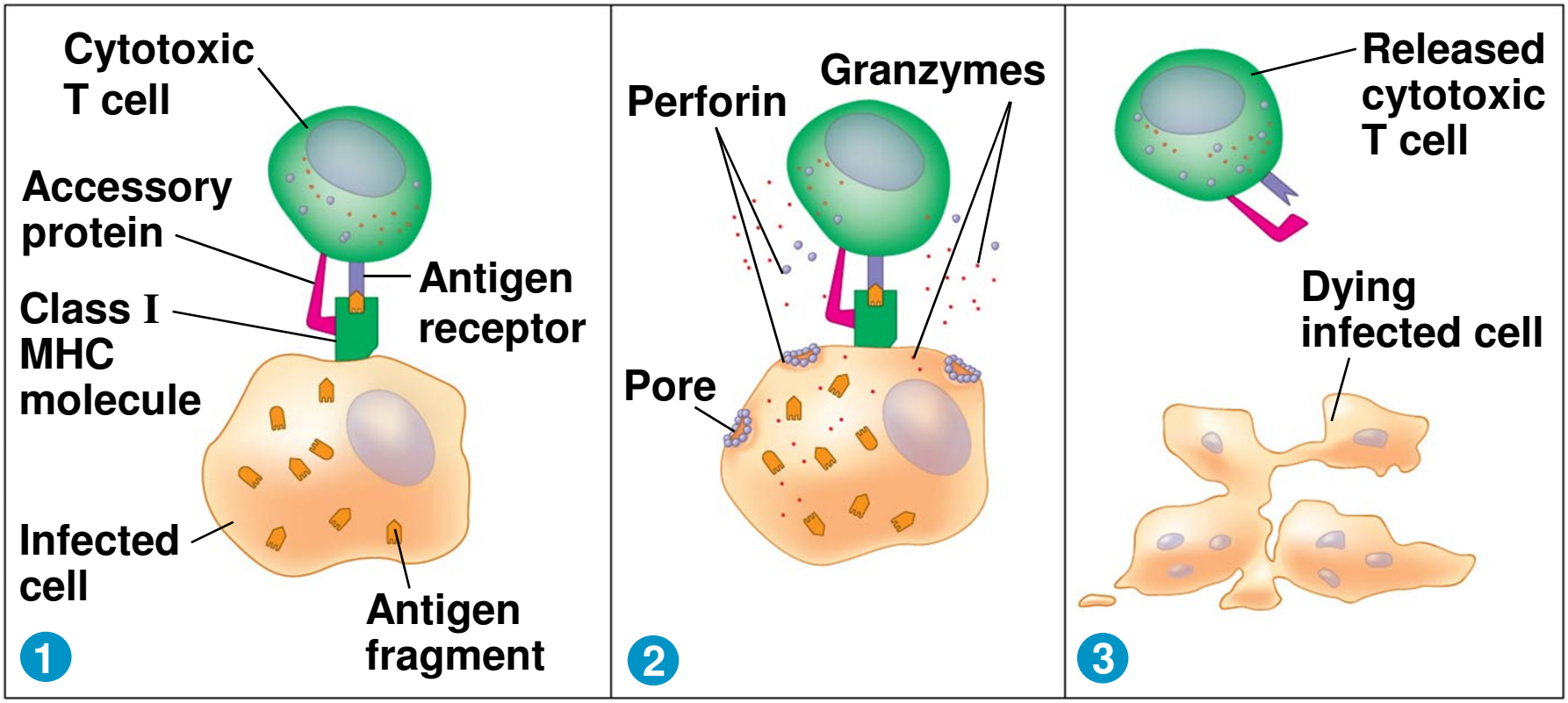
Animation: Helper T Cells
Right click slide / Select play

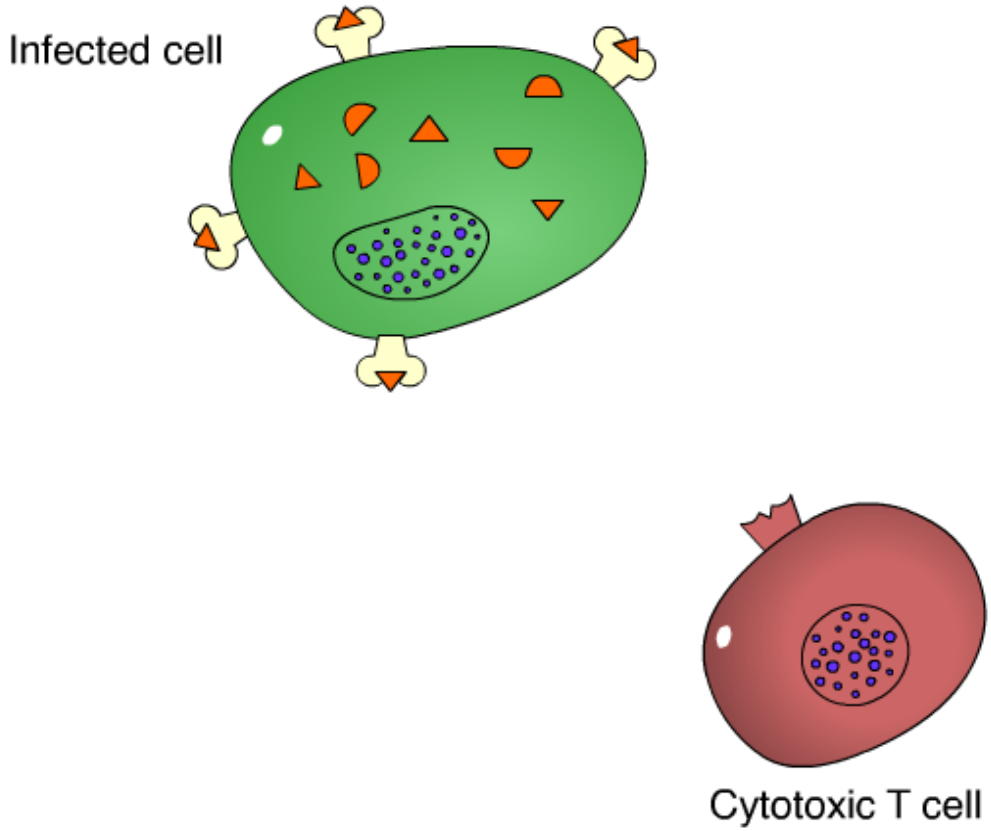
Cytotoxic T Cells: A Response to Infected Cells

- **Cytotoxic T cells** are the effector cells in the cell-mediated immune response
  - Require signals from helper T cells and interaction with an antigen-presenting cell to become active
- Targeted destruction of infected host cells!
  - Use toxic proteins to kill cells infected by intracellular pathogens
    - Disrupt the membranes of target cells and trigger apoptosis
    - Deprives pathogen of a place to reproduce
    - Exposes cell contents to antibodies

Figure 35.14-3



Cell-mediated Immunity

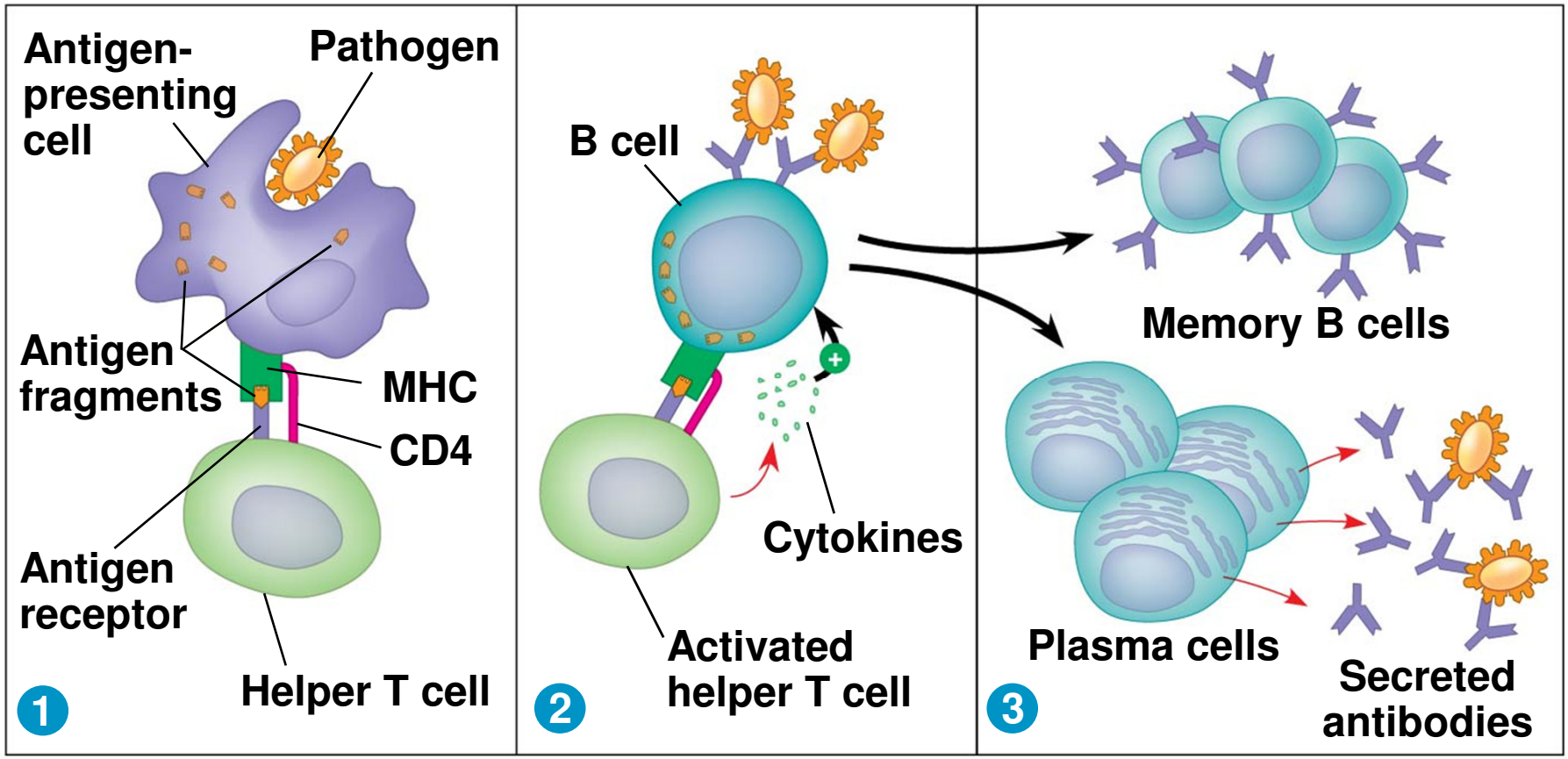


Animation: Cytotoxic T Cells
Right click slide / Select play

B Cells and Antibodies: A Response to Extracellular Pathogens

- The humoral response is characterized by secretion of antibodies by clonally selected B cells
- Activation of B cells involves helper T cells and proteins on the surface of pathogens
- In response to cytokines from helper T cells and an antigen, a B cell proliferates and differentiates into
  - Memory B cells
  - Antibody-secreting effector cells (**plasma cells**)
- Note: Antibodies do not kill pathogens
  - They mark pathogens for destruction to facilitate phagocytosis

Figure 35.15-3



Summary of the Humoral and Cell-Mediated Immune Responses

- Both the humoral and cell-mediated responses can include primary and secondary immune responses
- Memory cells enable the secondary response

Figure 35.16a

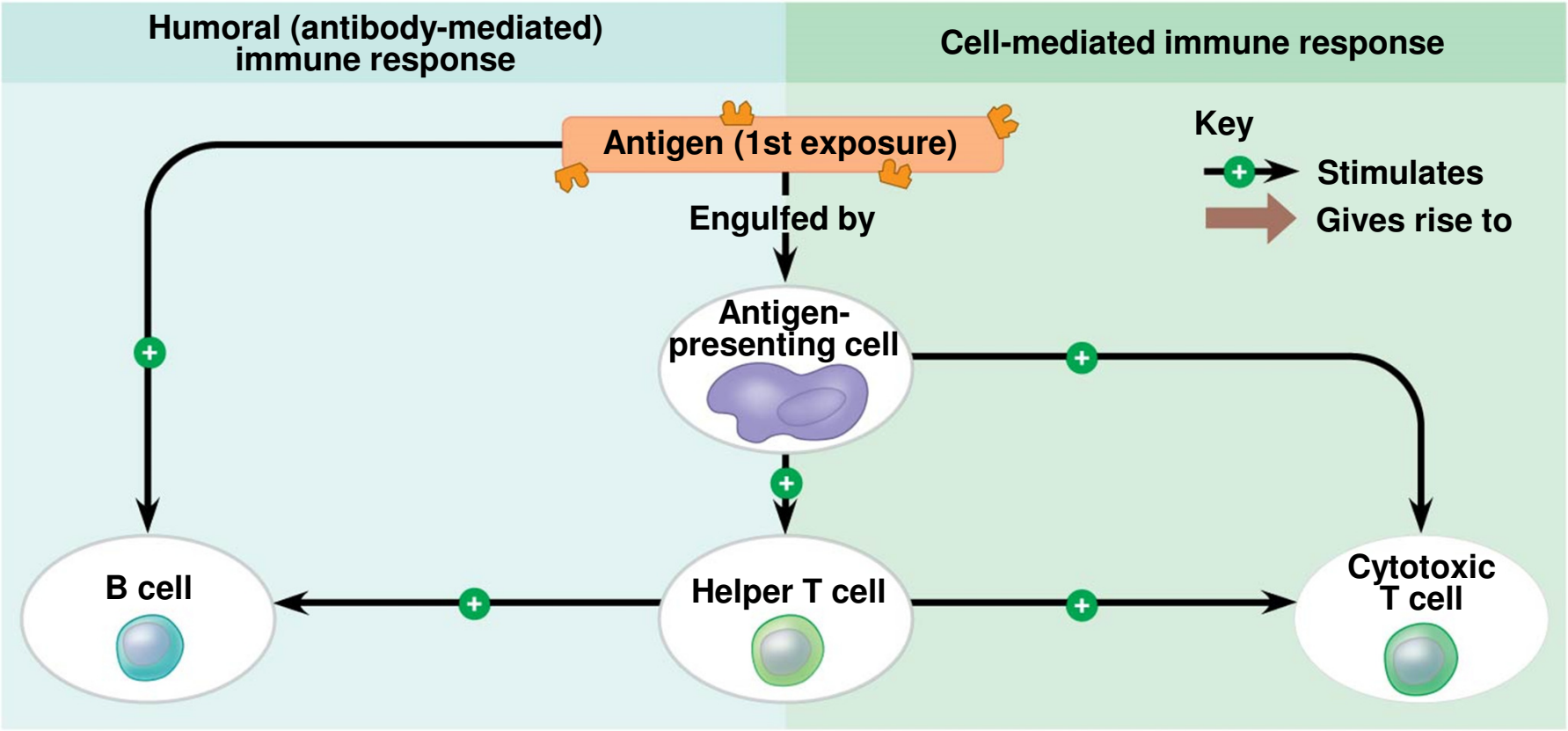
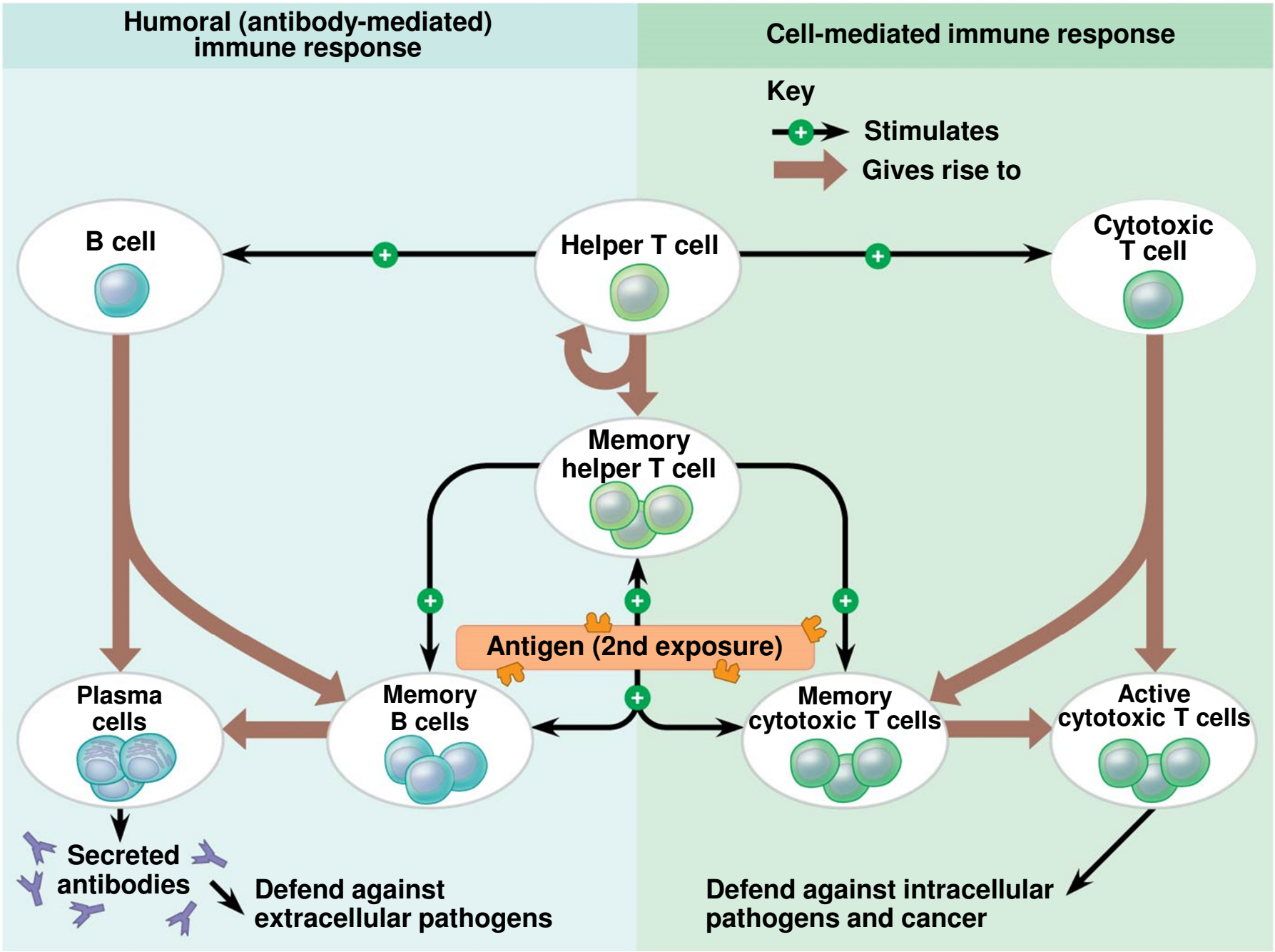


Figure 35.16b



Active and Passive Immunization

- **Active immunity** occurs naturally when a pathogen infects the body
- In **passive immunity**, antibodies in the recipient are produced by another individual
  - Provides immediate, short-term protection
  - Ex: Antibodies cross the placenta from mother to fetus or pass from mother to infant in breast milk
- Both active and passive immunity can be induced artificially

- Active immunity is induced when antigens are introduced into the body in *vaccines*
- In this process of **immunization**, inactivated bacterial toxins or weakened or killed pathogens are introduced
  - Induces a primary immune response and immunological memory
  - Any future encounter with the pathogen triggers a rapid and strong secondary immune response
- Passive immunity can be conferred artificially by injecting antibodies into a nonimmune person
  - Ex: Antivenin

Immune Rejection

- Cells transferred from one person to another can be attacked by the recipient's immune defenses
  - This complicates blood transfusions and the transplant of tissues or organs
- To minimize rejection, physicians use donor tissue that closely matches the MHC molecules of the recipient
- Recipients also take medicines that suppress their immune responses

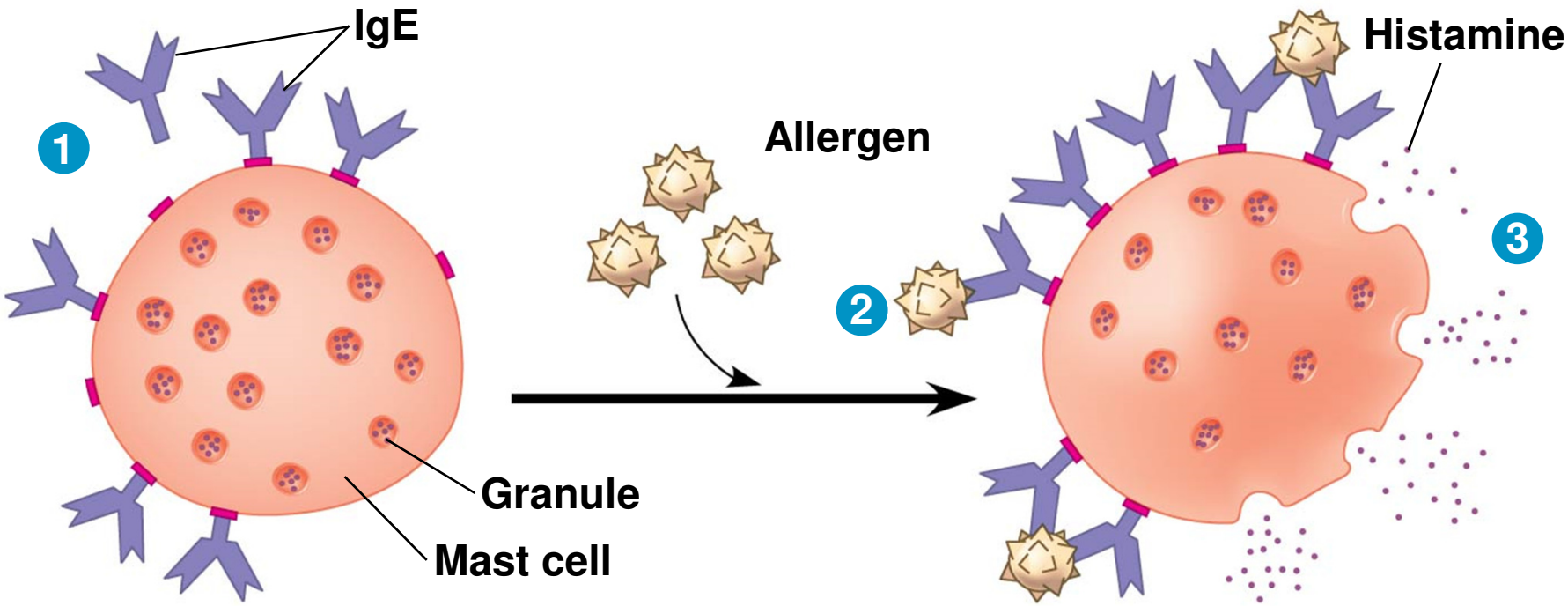
Disruptions in Immune System Function

- Although adaptive immunity offers significant protection against many pathogens, it is not fail-safe

Allergies

- Allergies are exaggerated (hypersensitive) responses to antigens called **allergens**
  - In localized allergies such as hay fever, plasma cells secrete antibodies specific for antigens on the surface of pollen grains
  - This triggers immune cells in connective tissue to release histamine and other inflammatory chemicals
- Antihistamines block receptors for histamine and diminish allergy symptoms

Figure 35.17



- An acute allergic response can lead to anaphylactic shock, a life-threatening reaction
- Substances that can trigger anaphylactic shock in allergic individuals include bee venom, penicillin, peanuts, and shellfish
- People with these hypersensitivities often carry epinephrine to counteract the allergic response

Autoimmune Diseases

- In individuals with **autoimmune diseases**, the immune system targets certain molecules of the body
- Autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, insulin-dependent diabetes mellitus, and multiple sclerosis

Immune System Avoidance

- Mechanisms to thwart immune responses have evolved in pathogens
- A pathogen may alter how it appears to the immune system by changing the epitopes it expresses
  - Called *antigenic variation*
  - Ex: Influenza virus
- Some viruses avoid an immune response by infecting cells and then entering an inactive state called *latency*
  - Remains latent until a stimulus, such as stress, fever, or menstruation, reactivates it
  - Ex: Herpes simplex virus

- Acquired immunodeficiency syndrome (AIDS) is caused by **HIV (human immunodeficiency virus)**, which both attacks and escapes the immune system
  - Infects helper T cells with high efficiency
    - Impairs humoral and cell-mediated responses
  - Escapes the immune system through its high mutation rate
    - Reduces the ability of the immune system to eliminate the infection
  - Can also undergo latency
- People with AIDS are highly susceptible to infections and cancers that a healthy immune system would normally defeat

Cancer and Immunity

- The frequency of certain cancers increases when adaptive immunity is impaired
- The immune system can act as a defense against viruses that cause cancer and against cancer cells that harbor viruses
- In 2006, a vaccine was released that acts against human papillomavirus (HPV)
  - A virus associated with cervical cancer